

# Heparin-Induced Thrombocytopenia

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# DVT in a Breast Cancer Patient

69-year-old woman, first Dx Breast Ca in 2002,  
on and off chemotherapy last 2 years for  
recurrent pleural metastases

First left leg DVT in March '06

July '06 Admitted for progressive leg pain and  
swelling, worse DVT, despite outpatient warfarin  
Rx IV heparin, IVC filter (platelets 350K)

Two weeks later: Discharged on warfarin (platelets  
81K; had been ~80K last several days)

# HIT With Cancer



# Some Lessons from this Case

- HIT is a common problem
- HIT engenders an extreme risk for serious thrombotic complications
- Unopposed warfarin increases this risk
- IVC filters should be avoided
- Alternative anticoagulants should be started expeditiously
- Therefore, clinicians must be highly informed and remain vigilant for HIT

There are more than 100 HIT stories  
in the Medical Center every year...



# Frequency of HIT

## Perspectives

- More than 1 trillion units heparin used yearly in US; 1/3 of hospitalized exposed (12 million)
- Unfractionated heparin – 3 - 5% incidence;  
Heart surgery 2.5% incidence
- LMWHeparin, Catheter-flushes -- ~0.5%
- Warkentin, NEJM '95, 11/332 SQ heparin v. 0/333 LMWH developed HIT
- Laster, 1988, 10/2,000 (0.5%) HIT exposed only to coated vascular catheter
- Frequency of thromboemboli – 30-75%

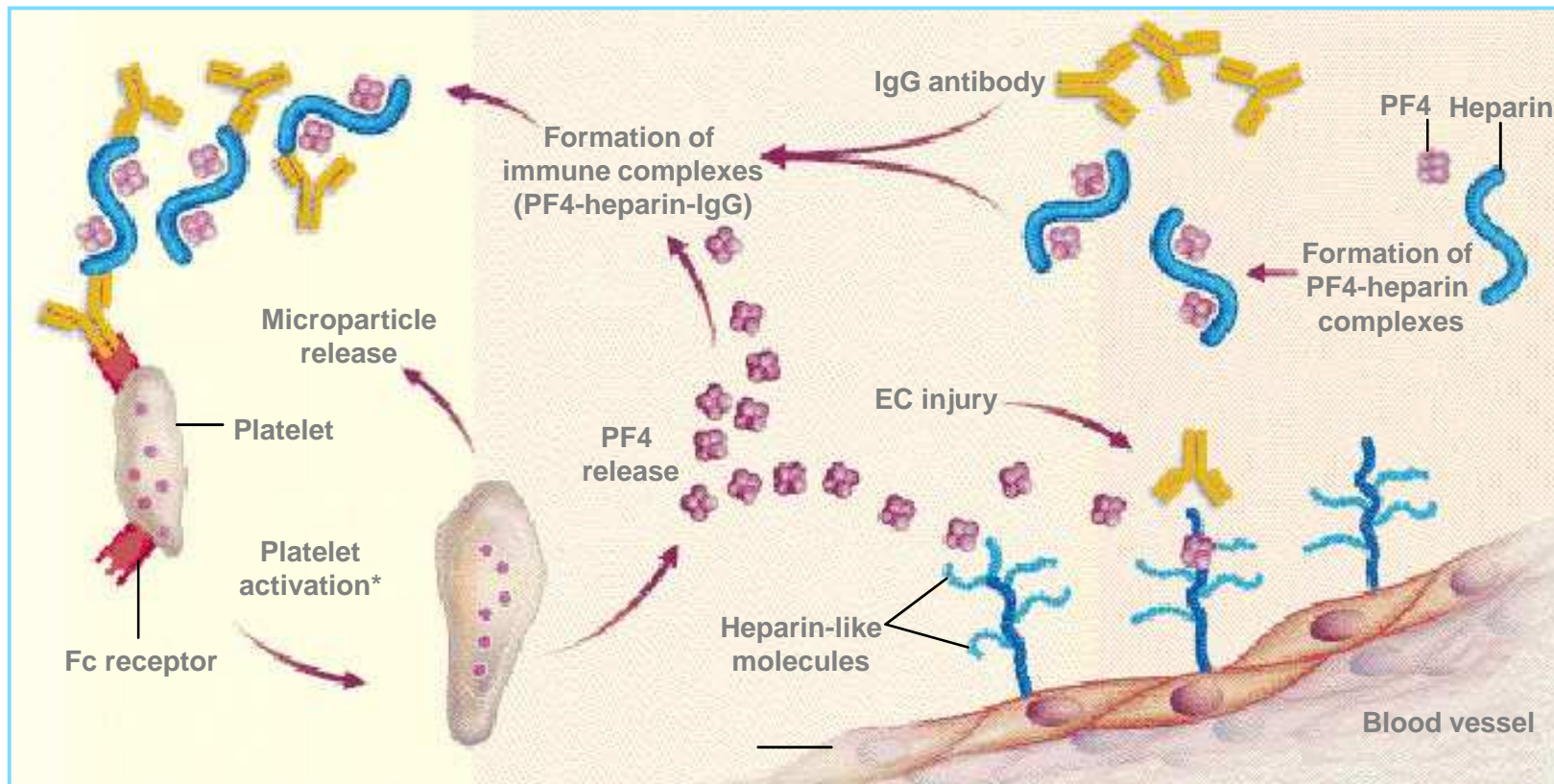
# Some Paradoxes of HIT

Heparin, the most powerful anticoagulant of the twentieth Century, saving uncountable lives and limbs, *also produces the most extreme hypercoagulable disorder, costing thousands yearly their lives and limbs.*

HIT, an immune reaction to an anticoagulant that lowers platelet count, rarely causes bleeding, *it causes thromboses, (and platelet transfusions are contraindicated).*

Health professionals should be knowledgeable about a reaction that is common, often catastrophic, preventable, treatable, iatrogenic, and a major source of litigation, *yet textbooks and medical curriculae pay little attention, and prevailing lack of awareness is shocking.*

# Heparin-Induced Thrombocytopenia (HIT): Pathophysiology<sup>1</sup>



\*Places patient at greater risk from primary thrombotic problem.

1. Adapted from Aster RH. *N Engl J Med.* 1995;332(20):1374-1376.

# Heparin-Induced Thrombocytopenia (HIT): Clinical Consequences if Untreated

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## Sequelae

## Incidence

New thromboses  
(arterial or venous)

~50%

Amputation

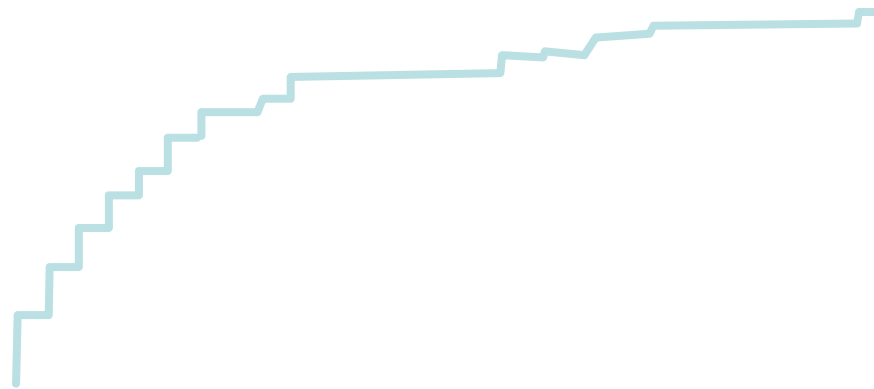
~21%

Death

~30%

# Risk of Thrombosis with HIT After Heparin is Stopped (if an effective alternative is not begun)

Cumulative  
frequency of  
thrombosis (%)



Days after isolated HIT recognized

# HIT is a Clinico-Pathologic Syndrome

- Fall in platelet counts (generally >50%)
- Appropriate time after heparin initiation (5-12 days)
- Extreme risk for venous or arterial thromboembolic complications

Eventually:

- Serologic confirmation of platelet-activating heparin-PF4 antibodies

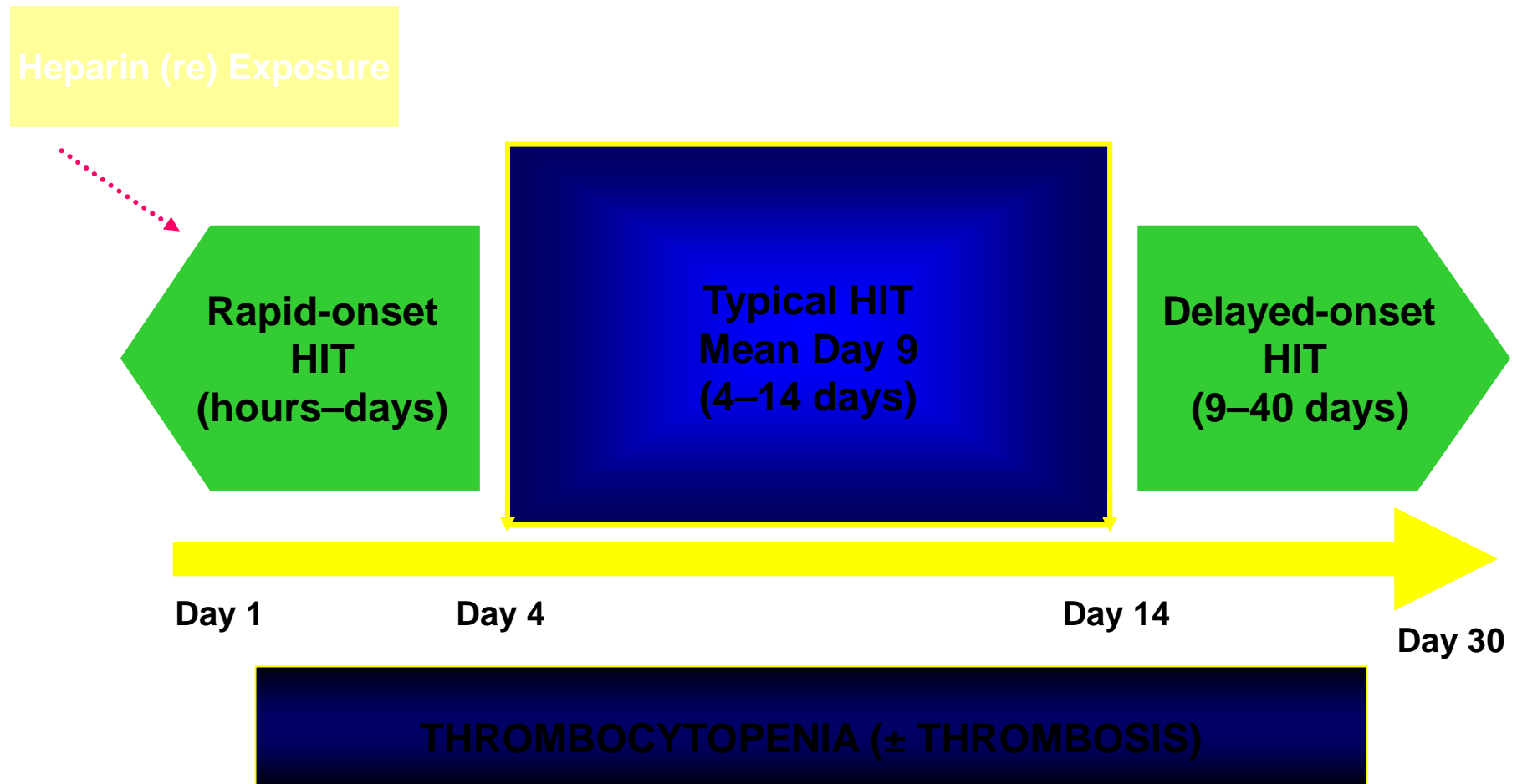
# Clinical Suspicion for HIT

## The 4 T's (Warkentin, 2003)

- Thrombocytopenia
  - Timing
  - Thrombosis
  - oTher causes for low platelets
- award 0–2 points for how typical for HIT
- high prob 6–8 pts; intermed 4-5; low 0-3

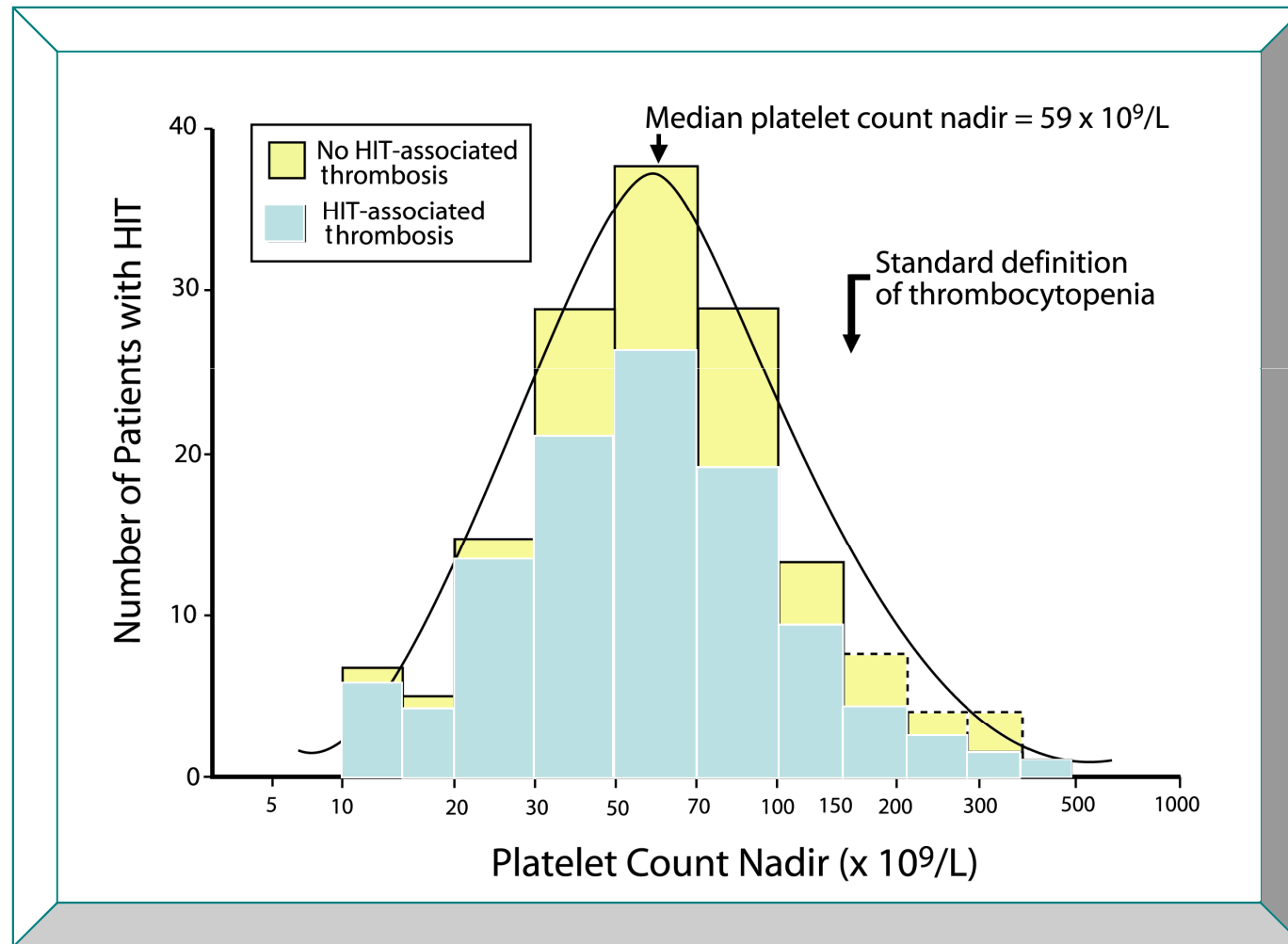
## The 5<sup>th</sup> T: The Test

# HIT Temporal Variants



*Courtesy of Dr Ahjad AlMahameed Cleveland Clinic, OH.*

# Distribution of Platelet Count



# Laboratory Tests for Heparin-PF4 Antibodies

- Commercially available ELISAs  
Highly sensitive (95-99%); High “false positive” rates; titer important
- Serotonin-release assays  
Technically demanding; variation lab-to-lab; limited availability
- Platelet aggregation assays  
Poor reproducibility
- Multiple others  
Flow cytometry or fluorescence-based  
Rapid bedside immunoassays
- Newer tests in development

# ACCP Antithrombotic Guidelines

## Chest supplement, Sept. 2004,

### Chapter on HIT: Monitoring, Dx and Rx

Examples of Evidence-Based Recommendations:

- “postoperative prophylaxis with UFheparin (HIT risk > 1%), at least every other day platelet count monitoring between post-op days 4-14 or until UFH is stopped (2C)”
- “postoperative prophylaxis with LMWheparin (HIT risk 0.1-1%), platelet count monitoring every 2 to 3 days between days 4-14 (2C)”

# Treatment of Other Drug-Induced Thrombocytopenias

- Stop the drug
- Consider platelet transfusions
- Consider other measures to reduce bleeding risk
- Once platelets rise, the reaction is over

## Treatment of Heparin- Induced Thrombocytopenia

- Stop all heparin exposures
- Initiate an alternative anticoagulant on suspicion
- Do NOT transfuse platelets; initiate warfarin early
- Risk of thrombosis extends weeks after platelet recovery



# Alternative Anticoagulants

Drug	Indications
Argatroban	FDA-approved for HIT (also for PCI)
Lepirudin	FDA-approved for HIT
Bivalirudin	PCI (including HIT patients)
Fondaparinux (pentasac.)	Prophylaxis and Rx of VTE
Danaparoid	Approved for HIT in Canada, Europe, Aust.

# The Key to Avoiding Catastrophes from HIT is Awareness, Vigilance, High Degree of Suspicion

**Consider HIT during/soon after heparin exposure\***

**When a patient...**

-  experiences a drop in platelet counts
-  develops thrombosis

*\* Heparin exposure may be through virtually any preparation (including LMWH), any dose, or any route of heparin (including flushes and coated lines)*

# HIT Summary

- A distinct clinico-pathologic syndrome
- Common—among most common causes of thrombocytopenia in hospital
- Serious, always potentially catastrophic
- Unique pathophysiology and testing
- Unique complication profile:  
Thromboemboli
- Unique management:  
alternative anticoagulants

# Proposed ICD-9 CM

- New Code
  - 289.84 Heparin-induced thrombocytopenia (HIT)
- A new 5 digit subclassification code as follows:
  - 287 Purpura and other hemorrhagic conditions
    - 287.4 Secondary thrombocytopenia
      - Post-transfusion purpura
      - Thrombocytopenia (due to):
        - » Dilutional
        - » Drugs
        - » Extracorporeal circulation of blood
        - » Platelet alloimmunization
      - Use addition E code to identify cause
    - Add **Excludes:** *Heparin-induced thrombocytopenia (289.84)*

# Proposed ICD-9 CM

- A new 5 digit subclassification code as follows:
  - 289 Other diseases of blood and blood-forming organs
    - 289.8 other specified diseases of blood and blood-forming organs
      - 289.81 Primary hypercoagulable state
      - 289.82 Secondary hypercoagulable state
      - Add **Excludes:** *Heparin-induced thrombocytopenia (289.84)*
      - 289.83 *Myelofibrosis*

## *New Code*

- 289.84 *Heparin-induced thrombocytopenia (HIT)*